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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/970,020	10/03/2001	Lirong Liu	107223-139 US	8697

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EXAMINER
JOYNES, ROBERT M

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 07/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/970,020	Applicant(s) LIU ET AL.	
	Examiner Robert M. Joynes	Art Unit 1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 May 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-54* is/are pending in the application.

4a) Of the above claim(s) *1-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Receipt is acknowledged of applicants' Amendment filed on May 8, 2003.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 24-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gilbert in combination with Baichwal et al. (US 4994276).

Gilbert teaches a bilayer tablet that has a controlled release and immediate release profile for tramadol (Page 1, lines, 25-31; Page 2, lines 17-37; Page 3, lines 1-3, 30-37; Page 4, lines 1-3, 13-37; Page 5, lines 1-9; Page 6, lines 30-35). The composition is controlled in such a way so as to reduce the adverse side effects of nausea and/or dizziness believed to be associated with the enantiomer (Page 5, lines 3-9). The dosage forms taught by Gilbert may be designed to release either of the enantiomers faster than the other, or before the other (Page 3, lines 30-37; Page 4,

lines 1-12). Further the dosage forms can be formulated to deliver the drugs at a constant rate for at least 8 hours preferably 12 hours and most preferably 24 hours (Page 3, lines 30-37). The release profiles taught in the specification and shown in the Figures teach the release profiles of the instant claims. Further Gilbert teaches that any conventional controlled-release technology can be used to achieve the desired tablet formulation. Gilbert does not expressly teach the heteropolysaccharide and polysaccharide gum excipient formulation. Gilbert does not expressly teach the exact ranges recited for the release profiles and the concentrations in the instant claims.

Baichwal teaches a free-flowing slow release excipient formulation comprising a heteropolysaccharide (xanthan gum), a polysaccharide (locust bean gum) and an inert filler (Col. 4, lines 7-67). This excipient formulation is used to achieve slow release profiles for a wide variety of drugs wherein the ratio of the drug to excipient is 1:3-7 and can be varied to achieve dissolution profiles for about 24 hours (Col. 9, lines 3-44). One type of drug that can be release in such a system is an analgesic (Col. 9, line 66 – Col. 10, line 6).

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to use the slow release excipient of Baichwal to prepare the controlled release portion of the bilayer tablet of Gilbert. Gilbert teaches any conventional controlled release system can be used to achieve the desired release profile for the analgesic tramadol. Baichwal teaches a gum excipient formulation that can be used in combination with analgesics that achieves a slow release profile depending on the ratio of drug to excipient used. It would be obvious to vary that ratio

to achieve the desired release profile for the composition. To vary the release profiles one of ordinary skill would vary the concentrations of the excipients used in the formulation.

While the reference does not teach the complete concentration range, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454, 105 USPQ 233, 235 (CCPA 1955).

One of ordinary skill in the art would have been motivated to do this to prepare a bilayer tablets in which releases an enantiomer of tramadol or any other recited drug over a 24 hours period such that the adverse side effects of the drug are reduced. One would be motivated to use the excipient system of Baichwal for the controlled release portion of the bilayer tablet because of its ability to be used with a wide variety of drugs, both soluble and insoluble as well as the inexpensive nature for producing a tablet with such a system. Further, the excipient system of Baichwal is inexpensive to manufacture and can be easily compressed into tablets which eliminates the use of expensive manufacturing equipment.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

Applicant's arguments filed May 8, 2003 have been fully considered but they are not persuasive. Applicants argue that no motivation exists to combine the teachings of Gilbert and Baichwal. Applicants cite that during a search they received over 22,000 hits for the words "controlled", "release" and "pharmaceutical" and they find no motivation to pick one reference out of 22,000. Finally, applicants state the Examiner is using improper hindsight reconstruction.

It is the position of the Examiner that proper motivation exists as stated above in the obvious type rejection. The primary reference teaches that a bi-layer tablet of different release profiles for enantiomers can be formed by using any conventional controlled-release technology to achieve the desired effect. The secondary reference teaches one such conventional controlled-release technology. This secondary reference further teaches that the excipient system can be used with a wide variety of drugs that are soluble and/or insoluble and that this system is less expensive in the preparation of the tablets. The Examiner cites these advantages as the motivation for combining the references.

As for applicants' recitation of search results, the Examiner finds these results very broad and unpersuasive. The Examiner does not doubt that applicants received over 22,000 hit when these three words were used as search terms. Applicants have not provided any evidence that all 22,097 references found by that search teach a controlled release system but rather have only shown that those three words appear in the same reference. These results are not persuasive.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert M. Joynes whose telephone number is (703) 308-8869. The examiner can normally be reached on Mon.-Thurs. 8:30 - 6:00, alternate Fri. 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (703) 308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3592 for regular communications and (703) 305-3592 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Robert M. Joynes
Patent Examiner
Art Unit 1615
July 22, 2003

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
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